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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	:	
GEORGE J. MURAKAWA, ET AL.	:	Group Art Unit: 1814
Filed: September 1, 1989	:	Examiner: M. Escallon
Serial No.: 07/402,450	:	
FOR: METHOD FOR AMPLIFICATION AND DETECTION OF RNA SEQUENCES	:	

APPLICANTS' REPLY BRIEF
PURSUANT TO 37 C.F.R. §1.193(b)

93-4018

Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

Sir:

NEW POINTS OF ARGUMENT

This Reply Brief addresses two new points of argument in the Examiner's Answer. In the ensuing quotations from the Answer, the new points of argument are underlined.

[1] Appellants argue that "Mullis et al. do not provide any 'RNA reference sequence' as required by step (ii)(b) of claim 18". This argument is not persuasive. Contrary to appellants' assertion, Mullis et al. disclose the amplification of viral RNA in the bridging sentences between columns 7 and 8. Also, is disclosed the alternative adding of either one or two primers so as to facilitate the amplification second strand target sequence followed by amplification of both strands by two primers, in column 9, lines 5-49 and column 10, line 47-57. Examiner agrees with appellants that Mullis et al. do not mention that one of the two amplified product[s] is used as "reference sequence". However, Mullis et al. do teach using two different primers to simultaneously amplify two

different sequences. Use of control to monitor success of analysis is notorious[ly] well known in the analytic arts. Appellants further argue that "no method for detecting false positive or negative data is taught or made obvious by Mullis et al.". This is not deemed to be persuasive because this is analysis and interpretation of the resulting product of the two sequences which is an expected result. [Answer, pp. 6-7; emphasis added]

[2] Appellants' argument that "the claimed invention requires simultaneously PCR amplification of viral RNA sample and at least one synthetic RNA sequence which does not include a preselected target sequence" is not clear because selection of a primer for the PCR process requires knowledge of the sequence to be amplified and knowledge of the sequence is required in order to produce a synthetic RNA sequence that is complementary to the probe in the hybridization of steps (iv) and (v). Furthermore, on page 4, lines 10-16 and page 6, lines 5-8 of the specification appellants refer to T-cell receptor and ß-actin gene sequences as the appropriate positive controls. [Answer, p. 7; emphasis added]

First New Point of Argument

(i) It is not apparent, in the portions of the reference cited by the Answer that "Mullis et al. do teach using two different primers [primer sets?] to simultaneously amplify two different sequences". This wrong statement in the Answer serves to emphasize the unobviousness of the invention defined, e.g., by independent claim 18 and the claims which depend from it.

(ii) The statement that the "Use of control to monitor success of analysis is notorious[ly] well known" is a new argument unsupported by any citation of any reference or by any affidavit in compliance with 37 C.F.R. §1.107(b). Applicants could not have "called for" such an affidavit previously because the argument is entirely new in the Answer.

Second New Point of Argument

This new argument is actually a contention that could be made only under 35 U.S.C. §112. However, all §112 rejections are "withdrawn" (Answer, p. 2).

This new §112 argument is difficult to understand.

The statement quoted in the Answer appears at page 7 of the brief which states:

> [T]he claimed invention requires simultaneous PCR amplification of viral RNA sample and at least one synthetic RNA sequence which does not include a preselected target sequence.

This statement corresponds to step (ii) of claim 18:

> (ii) simultaneously subjecting
>
> (a) said sample and
>
> (b) at least one synthetic RNA reference sequence which does not include said target sequence or which includes substantially more nucleotides than said target sequence or which includes at least about 20 nucleotides less than said target sequence
>
> to polymerase chain reaction amplification under conditions appropriate to simultaneously amplify said target sequence if present in said sample and said reference sequence;

The sequence of the "viral target" and of the RNA reference sequence are each known a priori. Hence, the sequences of the involved primers and probes are also known--and set forth in portions of the specification cited by the Answer.

Respectfully submitted,

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